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CURRENT TOPIC / АКТУЕЛНА ТЕМА

Historical and statistical aspects of risk groups analysis and testing in the context of gestational diabetes mellitus

Maja Macura[1,2], Stefan Dugalić[1,2], Jovana Todorović[3], Bojana Gutić[4], Miloš Milinčić[2], Dragana Božić[1], Milica Stojiljković[2,5], Ivan Soldatović[6], Igor Pantić[7], Milan Perović[2,8], Biljana Parapid[2,9], Miroslava Gojnić[1,2]

[1]University Clinical Centre of Serbia, Clinic for Gynecology and Obstetrics, Belgrade, Serbia;
[2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[3]University of Belgrade, Faculty of Medicine, Institute of Social Medicine, Belgrade, Serbia;
[4]University of Novi Sad, Institute of Oncology of Vojvodina, Clinic for Operative Oncology; Novi Sad, Serbia;
[5]University Clinical Centre of Serbia, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Belgrade, Serbia;
[6]University of Belgrade, Faculty of Medicine, Institute of Medical Statistics and Informatics, Belgrade, Serbia;
[7]University of Belgrade, Faculty of Medicine, Institute of Medical Physiology, Belgrade, Serbia;
[8]Narodni front University Clinic for Gynecology and Obstetrics, Belgrade, Serbia;
[9]University Clinical Centre of Serbia, Division of Cardiology, Belgrade, Serbia

SUMMARY
In order to enhance cost-benefit value of the gestational diabetes mellitus screening (GDM) the concept of universal screening i.e., screening of all pregnant women for gestational diabetes, has mostly been abandoned in favor of the concept of selective screening. Selective screening implies that only women with risk factors are being screened for GDM. However, some recent studies have shown that with the application of the selective screening approach, some women with GDM may not receive proper and timely diagnosis. This review addresses the pros and cons of both concepts. It will also discuss screening methods and methods of preparation and performance of oral glucose tolerance test and the interpretation of its results.
Keywords: gestational diabetes mellitus; universal screening; selective screening; oral glucose tolerance test

INTRODUCTION

In order to reduce the burden on the health system due to screening for gestational diabetes mellitus (GDM) for all pregnant women – universal screening, the concept of selective screening for GDM was developed. Selective screening, based on data from personal and family history, aims to identify a high-risk population for diabetes [1]. Some recent studies have shown the universal screening approach to be cost-effective [2]. In this review, we aim to present advantages and disadvantages of universal and selective screening for GDM.

Selective screening approach

The selective approach to screening is based on the definition of the evidence-based risk factors for the development of GDM. Age, race, and body mass index (BMI) were identified as risk factors associated with GDM, but also some other factors like polycystic ovarian syndrome [1, 3], but this association is not confirmed in all studies [4]. Adverse pregnancy outcomes (APOs) of previous pregnancies are associated with GDM and type 2 diabetes [5].

Previous studies have shown that when relying on the assessment for the GDM risk from the patient history half of the pregnant women with GDM do not provide data on the existence of the risk factors, while half of the healthy pregnant women have one or more risk factors [6].

When deciding on the recommendations for universal or selective GDM screening it is necessary to define the population that should be screened, the recommended screening methods and their timing, as well as the treatment modalities and the follow-up [7].

Adverse pregnancy outcomes

Although a systematic review of the existing studies has shown the association of the GDM according to the criteria from the World Health Organization (WHO) and according to the International Association for Diabetes in Pregnancy Study Group (IADPSG) criteria with APOs, the value of glycemia that has significant implications for pregnancy is still to be defined [8]. Preexisting diabetes is associated with the risk of having a child with congenital anomalies, and the risk is related to

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Correspondence to:
Jovana TODOROVIĆ
University of Belgrade
Faculty of Medicine
Institute of Social Medicine
Dr. Subotica 15
11000 Belgrade
Serbia
jovana.todorovic@med.bg.ac.rs

hyperglycemia during embryogenesis [8]. GDM does not carry an increased risk for congenital anomalies of the fetus [9]. Pregnancy complicated by diabetes carries the risk of fetal growth disorders, birth complications, and perinatal asphyxia.

The effects of the timely treatment on the APOs also remain undefined, and although it was shown that the treatment of GDM reduces the likelihood of macrosomia, preeclampsia, and shoulder dystocia, the effects of the GDM treatment on metabolic abnormalities in newborns and APOs is still to be examined further [10].

Methods of screening and diagnosing

Oral glucose tolerance tests are cumbersome to perform, and their reproducibility is low. The determination of only glycosylated hemoglobin and fructosamine cannot identify a lesser degree of glycoregulation disorders in type 2 diabetes and GDM [11]. The study that examined the cost-effectiveness of the universal GDM screening using the IADPSG showed that, although this screening is more costly, it may be cost-effective under certain conditions [12]. More recent systematic review showed that although treatment of GDM is cost-effective, universal screening does not seem to be [13].

When deciding on the implementation of a screening program, its potential flaws, i.e., side effects, must be evaluated. One of the disadvantages of GDM screening is that pregnant women with GDM are more likely to have cesarean deliveries, even with eutrophic children [14]. This could imply that the GDM diagnosis in the pregnant women can motivate obstetricians towards easier decision-making about caesarean section [15]. The higher frequency of operative delivery in GDM, with normal newborns' weight, may also be a consequence of perinatal asphyxia.

In a population where the prevalence of type 2 diabetes and GDM is high, the number of women at low risk is small. Selective screening reduces the number of tested persons by 34.6%, without reducing GDM detection rates [16]. That is why the American Diabetes Association (ADA) changed its original position of promoting universal screening, to the current position of selective GDM screening based on risk factors [1, 3]. ADA guidelines mandate screening of high-risk populations at the first prenatal visit (pronounced obesity, if she had GDM in one of the previous pregnancies, glycosuria in pregnancy, or type 2 diabetes in the family history). Low risk is determined by age under 25 years, belonging to ethnic and racial groups with a low prevalence of diabetes, a negative history of diabetes in the immediate family, normal weight gain in the current pregnancy and an unencumbered obstetric history. If she does not meet the stated criteria of one of the two mentioned groups, the patient is classified in the group of women with a moderate risk of developing GDM. Women at high risk should be tested as soon as possible. If the initial test is negative, it should be repeated between the 24th to the 28th week of pregnancy. There are two approaches to the diagnosis of GDM in high-risk individuals, the so-called "one step approach" and "two step approach." The first one uses only one "step" in establishing the diagnosis- an oral glucose tolerance test (OGTT). The second one has two "steps." The first step is screening with an oral glucose challenge test (GCT) with 50 g of glucose, and in case of poor values, (glucose after one hour of more than 11mmol/l), a definitive, diagnostic OGTT is performed.

It was shown that screening based on risk factors will reduce the number of women tested but will result in an increase in the number of pregnant women with the missed GDM diagnosis [17]. This is in contrast to the findings of the study by Naylor et al, who did not register a reduction in GDM detection rates. Variations in the prevalence of GDM and risk factors in different populations will lead to variations in the implications of selective screening in different epidemiological settings [18]. Therefore, decisions on acceptable screening detection rates and false negative values will remain in the domain of national organizations. In a retrospective study comparing universal and selective screening (based on high risk using ADA criteria), 18,000 patients were examined [19]. If only high-risk patients were screened, 3% of women would remain with undiagnosed GDM. In this population, only 10% of women were in the low-risk category and for them screening would be waived. Failure to properly apply algorithms in a high-risk population is likely to result in a relatively large number of undiagnosed cases compared to unconfirmed cases in a low-risk population [20].

We still do not have the results from the randomized controlled trials (RCTs) that the higher detection rates of GDM lead to lower prevalence of APOs [21]. The most common GDM screening method involves an oral GCT with 50 g of glucose, the so-called O'Sullivan's test or GCT, which was promoted by O'Sullivan and Mahan [22]. It involves the oral consumption of a solution containing 50 g of glucose, regardless of the time of the previous meal. One hour later, glycemia is determined. The most common cut-off value is 7.77 mmol/l (140 mg/dl), which is usually around 15% of positive test results [23]. By reducing this value to 7.22 mmol/l (130 mg/dl), the sensitivity of the test is significantly improved [21].

GCT shows sensitivity of 80% and specificity of 90%. This means that as many as 20% of patients undergoing GCT remain undiagnosed [24, 25]. GCT has been criticized as poorly repeatable, unpleasant, impractical to perform, relatively expensive and time-consuming [26], with low specificity [27].

Pregnant women with a positive screening for GDM require the use of a diagnostic test, which is an oral glucose load test (with 75 or 100 g) – OGTT. Currently, the two-step approach is recommended by the ADA and American College of Obstetricians (ACOG) with the ADA recommending Carpenter Coustan or IADPSG criteria for diagnosis of GDM, while ACOG recommends the Carpenter Coustan or National diabetes data group criteria. IADPSG, WHO and International Federation of Gynecology and Obstetrics recommend the one-step approach [21].

Criteria for diagnosis

The different criteria define different values for the assessment of the positive test and for the establishment of the GDM diagnosis [21]. Studies have shown that if even one value is increased, the risk of macrosomic growth of the fetus and the complications that accompany it is increased [28, 29].

Glycoregulation is strongly influenced by placental hormones, so special changes are expected in twin pregnancy. In these pregnant women, a significant difference was found in fasting glycemia values. The frequency of GDM in twin pregnancies is higher.

This article was written in accordance with the ethical standards of the institutions and the journal.

CONCLUSION

Selective, unlike universal screening for GDM aims to identify a high-risk population for diabetes. In a population where the prevalence of type 2 diabetes and GDM is high, the number of women at low risk is small, so universal screening is more effective. Decisions on acceptable screening should remain in the domain of national organizations, which will adapt the decision to the characteristics of the population. The most common GDM screening method involves an oral GCT with 50 g of glucose.

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REFERENCES

1. Gojnic Dugalic M., et al. Diabetes i trudnoća. Medicinski fakultet Univerziteta u Beogradu: Novo doba, 2012.
2. Benhalima K, Van Crombrugge P, Moyson C, Verhaeghe J, Vandeginste S, Verlaenen H, et al. Risk factor screening for gestational diabetes mellitus based on the 2013 WHO criteria. Eur J Endocrinol. 2019;180(6):353–63. [DOI: 10.1530/EJE-19-0117] [PMID: 31120231]
3. Committee ADAPP. 15. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes—2022. Diabetes Care. 2021;45(Supplement_1):S232–43. [DOI: 10.2337/dc22-S015] [PMID: 34964864]
4. Li X, Liu X, Zuo Y, Gao J, Liu Y, Zheng W. The risk factors of gestational diabetes mellitus in patients with polycystic ovary syndrome: What should we care. Medicine (Baltimore). 2021;100(31):e26521. [DOI: 10.1097/MD.0000000000026521] [PMID: 34397795]
5. Miller C, Lim E. The risk of diabetes after giving birth to a macrosomic infant: data from the NHANES cohort. Matern Heal Neonatol Perinatol. 2021;7(1):12. [DOI: 10.1186/s40748-021-00132-8] [PMID: 33980302]
6. Bashir M, Ibrahim I, Eltaher F, Beer S, Baagar K, Aboulfotouh M, et al. Screening pregnant women in a high-risk population with WHO-2013 or NICE diagnostic criteria does not affect the prevalence of gestational diabetes. Sci Rep. 2021;11(1):5604. [DOI: 10.1038/s41598-021-84918-y] [PMID: 33692395]
7. Liao LD, Ferrara A, Greenberg MB, Ngo AL, Feng J, Zhang Z, et al. Development and validation of prediction models for gestational diabetes treatment modality using supervised machine learning: a population-based cohort study. BMC Med. 2022;20(1):307. [DOI: 10.1186/s12916-022-02499-7] [PMID: 36104698]
8. Alexopoulos AS, Blair R, Peters AL. Management of Preexisting Diabetes in Pregnancy: A Review. JAMA. 2019;321(18):1811–9. [DOI: 10.1001/jama.2019.4981] [PMID: 31087027]
9. Farrell T, Neale L, Cundy T. Congenital anomalies in the offspring of women with type 1, type 2 and gestational diabetes. Diabet Med. 2002 ;19(4):322–6. [DOI: 10.1046/j.1464-5491.2002.00700.x] [PMID: 11943005]
10. Behboudi-Gandevani S, Bidhendi-Yarandi R, Panahi MH, Vaismoradi M. The Effect of Mild Gestational Diabetes Mellitus Treatment on Adverse Pregnancy Outcomes: A Systemic Review and Meta-Analysis. Front Endocrinol (Lausanne). 2021;1212:640004. [DOI: 10.3389/fendo.2021.640004] [PMID: 33841332]
11. Mendes N, Alves M, Andrade R, Ribeiro RT, Papoila AL, Serrano F. Association between glycated albumin, fructosamine, and HbA1c with neonatal outcomes in a prospective cohort of women with gestational diabetes mellitus. Int J Gynaecol Obstet. 2019;146(3):326–32. [DOI: 10.1002/ijgo.12897] [PMID: 31242319]
12. Cheung NW, Jiang S, Athayde N. Impact of the IADPSG criteria for gestational diabetes, and of obesity, on pregnancy outcomes. Aust N Z J Obstet Gynaecol. 2018;58(5):553–9. [DOI: 10.1111/ajo.12772] [PMID: 29359312]
13. Fitria N, van Asselt ADI, Postma MJ. Cost-effectiveness of contolling gestational diabetes mellitus: a systematic review. Eur J Health Econ. 2019;20(3):407–17. [DOI: 10.1007/s10198-018-1006-y] [PMID: 30229375]
14. Coustan DR, Widness JA, Carpenter MW, Rotondo L, Pratt DC, Oh W. Should the fifty-gram one-hour glucose screening test for gestational diabetes be administered in the fasting or fed state? Am J Obstet Gynecol. 1986;154(5):1031–5. [DOI: 10.1016/0002-9378(86)90744-1] [PMID: 3706427]
15. Maulik D, Lysikiewicz A, Sicuranca G. Umbilical arterial Doppler sonography for fetal surveillance in pregnancies complicated by pregestational diabetes mellitus. J Matern Fetal Neonatal Med. 2002;12(6):417–22. [DOI: 10.1080/jmf.12.6.417.422] [PMID: 12683654]
16. Benhalima K, Van Crombrugge P, Moyson C, Verhaeghe J, Vandeginste S, Verlaenen H, et al. Risk factor screening for gestational diabetes mellitus based on the 2013 WHO criteria. Eur J Endocrinol. 2019;180(6):353–63. [DOI: 10.1530/EJE-19-0117] [PMID: 31120231]
17. Vitacolonna E, Succurro E, Lapolla A, Scavini M, Bonomo M, Di Cianni G, et al. Guidelines for the screening and diagnosis of gestational diabetes in Italy from 2010 to 2019: critical issues and the potential for improvement. Acta Diabetol. 2019;56(11):1159–67. [DOI: 10.1007/s00592-019-01397-4] [PMID: 31396699]
18. Kattini R, Hummelen R, Kelly L. Early Gestational Diabetes Mellitus Screening With Glycated Hemoglobin: A Systematic Review. J Obstet Gynaecol Can. 2020;42(11):1379–84. [DOI: 10.1016/j.jogc.2019.12.015] [PMID: 32268994]
19. Nwali SA, Onoh RC, Dimejesi IB, Obi VO, Jombo SE, Edenya OO. Universal versus selective screening for gestational diabetes mellitus among antenatal clinic attendees in Abakaliki: using the one-step 75 gram oral glucose tolerance test. BMC Pregnancy Childbirth. 2021;21(1):735. [DOI: 10.1186/s12884-021-04168-8] [PMID: 34715805]
20. American Diabetes Association. 14. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-2020. Diabetes Care. 2020 Jan;43(Suppl 1):S183–S192. [DOI: 10.2337/dc20-S014] [PMID: 31862757]
21. Minschart C, Beunen K, Benhalima K. An Update on Screening Strategies for Gestational Diabetes Mellitus: A Narrative Review. Diabetes, Metab Syndr Obes. 2021;14:3047–76. [DOI: 10.2147/DMSO.S287121] [PMID: 34262311]
22. O'Sullivan JB, Mahan C. Criteria for the oral glucose tolerance test in pregnancy. Diabetes 1964;13:278–85. [PMID: 14166677]
23. Bonomo M, Gandini ML, Mastropasqua A, Begher C, Valentini U, Faden D, et al. Which cutoff level should be used in screening for glucose intolerance in pregnancy? Am J Obstet Gynecol. 1998;179(1):179–85. [DOI: 10.1016/s0002-9378(98)70270-4] [PMID: 9704785]
24. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. Am J Obstet Gynecol. 1982;144(7):768–73. [DOI: 10.1016/0002-9378(82)90349-0] [PMID: 7148898]

25. Berger H, Mathew S. Counterpoint: Selective Screening for Gestational Mellitus. 2009;32(7):1352–4. [DOI: 10.2337/dc09-0361] [PMID: 19564480]
26. Sert UY, Ozgu-Erdinc AS. Gestational Diabetes Mellitus Screening and Diagnosis. Adv Exp Med Biol. 2021;1307:231–55. [DOI: 10.1007/5584_2020_512] [PMID: 32314318]
27. Montagna M, Lippi G, Targher G, Fava C, Guidi GS. Glucose Challenge Test Does Not Predict Gestational Diabetes Mellitus. Inter Med. 2008;47(13):1171–4. [DOI: 10.2169/internalmedicine.47.0930] [PMID: 18591836]
28. Lindsay MK, Graves W, Klein L. The relationship of one abnormal blood glucose tolerance test value and pregnancy complications. Obstet Gynecol. 1989;73(1):103–6. [PMID: 2909030]
29. Succurro E, Fraticelli F, Franzago M, Fiorentino TV, Andreozzi F, Vitacolonna E, et al. Hyperglycemia at 1h-OGTT in Pregnancy: A Reliable Predictor of Metabolic Outcomes? Front Endocrinol (Lausanne). 2021;12:612829. [DOI: 10.3389/fendo.2021.612829] [PMID: 34108933]

Историјски и статистички аспект анализе ризичних група и тестирања у контексту гестацијског дијабетеса мелитуса

Маја Мацура[1,2], Стефан Дугалић[1,2], Јована Тодоровић[3], Бојана Гутић[4], Милош Милинчић[2], Драгана Божић[1], Милица Стојиљковић[2,5], Иван Солдатовић[6], Игор Пантић[7], Милан Перовић[2,8], Биљана Парапид[2,9], Мирослава Гојнић[1,2]

[1]Универзитетски клинички центар Србије, Клиника за гинекологију и акушерство, Београд, Србија;
[2]Универзитет у Београду, Медицински факултет, Београд, Србија;
[3]Универзитет у Београду, Медицински факултет, Институт за социјалну медицину, Београд, Србија;
[4]Универзитет у Новом Саду, Клиника за оперативну онкологију, Институт за онкологију Војводине, Нови Сад, Србија;
[5]Универзитетски клинички центар Србије, Клиника за ендокринологију, дијабетес и болести метаболизма, Београд, Србија;
[6]Универзитет у Београду, Медицински факултет, Институт за медицинску статистику и информатику, Београд, Србија;
[7]Универзитет у Београду, Медицински факултет, Институт за медицинску физиологију, Београд, Србија;
[8]Универзитетска клиника за гинекологију и акушерство „Народни фронт", Београд, Србија;
[9]Универзитетски клинички центар Србије, Клиника за кардиологију, Београд, Србија

САЖЕТАК

У циљу повећања исплативости скрининга гестацијског дијабетеса мелитуса, концепт универзалног скрининга, односно скрининга свих трудница на гестацијски дијабетес, углавном је напуштен у корист концепта селективног скрининга. Селективни скрининг подразумева да само жене са факторима ризика за гестацијски дијабетес мелитус подлежу процесу скрининга. Ипак, неке скорашње студије су показале да ако се примени селективни приступ скринингу, одређени проценат жена са гестацијским дијабетесом мелитусом не добије дијагнозу или је не добије правовремено. Овај прегледни рад се бави предностима и недостацима и једног и другог концепта. Методе скрининга и методе припреме и извођења оралног теста толеранције на глукозу, као и интерпретација његових резултата биће детаљније објашњени.

Кључне речи: гестацијски дијабетес мелитус; универзални скрининг; селективни скрининг; орални тест толеранције на глукозу